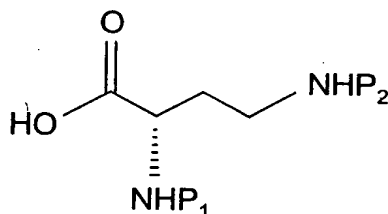


## WHAT IS CLAIMED IS:

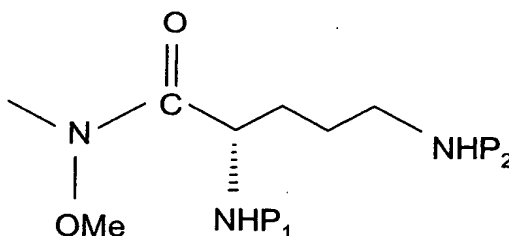
1. A process for preparing (S,S)-cis-2-phenyl-3-amino-piperidine which comprises:

(a) reacting the amino acid, L-ornithine or salt having a protecting group on the amino group on the  $\alpha$ -carbon and the amino group on the  $\delta$ -carbon thereof, having the

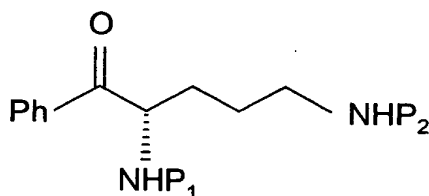
5 formula



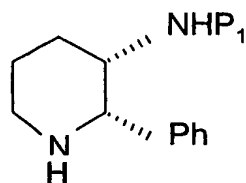
with N-methoxy-N-methylamino or salt thereof under amide forming conditions to produce an amide of the formula in the S configuration



10 (b) adding said amide to an effective amount of a Grignand reagent of the formula Ph MgX to form a ketone of the formula in the S configuration



(c) selectively deprotecting the amino group on the  $\delta$  carbon under conditions sufficient to cyclize said ketone to form a cyclic imine and reducing the resulting imine  
15 to form a product of the formula in the (S,S) configuration



and

(d) removing the protecting group on the  $\alpha$ -carbon to form said (S,S)-cis-2-phenyl-3-aminopiperidine, wherein

$P_1$  and  $P_2$  are different amino protecting groups, which are removed under  
5 different reaction conditions and

X is halide.

2. The process according to Claim 1 which additionally comprises differentially  
protecting the amino groups on the  $\alpha$  and  $\delta$  carbon atoms on the L-ornithine or salt  
10 thereof prior to step (a).

3. The process according to Claim 2 wherein the amino group on the  $\delta$ -carbon is  
protected by a group that can be removed by hydrogenolysis.

15 4. The process according to Claim 2 wherein the protecting group on the amino group  
on the  $\delta$ -carbon is benzyloxycarbonyl or dithiasuccinoyl.

5. The process of Claim 2 wherein differentially protecting the  $\alpha$  and  $\delta$  amino groups  
comprises:

20 (a) reacting the L-ornithine with a copper salt to form a copper complex with the  
amino group on the  $\alpha$ -carbon,

- (b) adding a protecting group to the amino group on the  $\delta$  carbon,
- (c) de-complexing the copper, and
- (d) protecting the amino group on the  $\alpha$ -carbon.

5     6. The process of Claim 5 wherein the copper salt is copper sulfate pentahydrate.

7. The process of Claim 1 wherein the amino group on the  $\delta$  carbon is protected by CBZ.

10    8. The process according to Claim 1 wherein in step (a) base is additionally present.

9. The process according to Claim 8 wherein the base is triethylamine, diisopropyl ethylamine, 2,6-lutidine, N, N,N', N'-tetramethylethylenediamine, potassium carbonate, lithium carbonate, sodium hydroxide, potassium hydroxide or N-methylmorpholine.

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10. The process according to Claim 1 wherein the Grignard reagent is phenyl magnesium bromide, phenyl magnesium chloride or phenyl magnesium iodine.

11. The process according to Claim 1 wherein from 3-6 equivalents of Grignard reagent  
20    is used per amide.

12. The process according to Claim 11 wherein about 4.0 to about 4.5 equivalents of Grignard reagent is used relative to the amide.

13. The process of Claim 1 wherein the reduction of the cyclic imine is effected by catalytic hydrogenation.

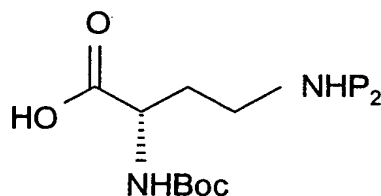
5 14. The process of Claim 13 wherein the catalyst is palladium on carbon.

15. The process of Claim 13 wherein the reduction of the cyclic imine is conducted in a solvent and the solvent is methanol.

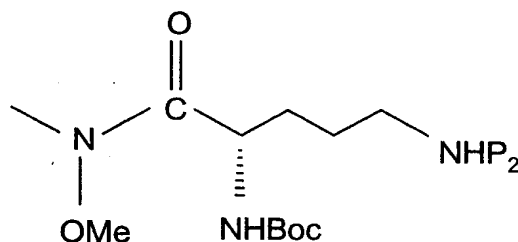
10 16. The process of Claim 1 wherein the deprotection of the amino group on the  $\delta$  carbon is performed at the same time as imine formation and reduction.

17. A process for preparing (S,S)-cis-2-phenyl-3-tertbutoxycarbonylaminopiperidine which comprises

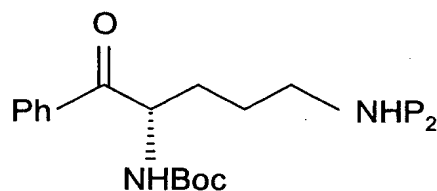
15 (a) reacting the amino acid, L-ornithine or salt thereof having a Boc protecting group on the amino group on the  $\alpha$ -carbon and a protecting group on the amino group on the  $\delta$  carbon thereof, having the formula:



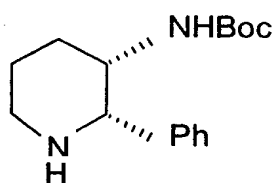
with N-methoxy-N-methylamino or salt thereof under amide forming conditions to  
20 produce an amide of the formula in the S configuration



(b) adding said amide to an effective amount of a Grignand reagent of the formula  $\text{Ph MgX}$  to form a ketone of the formula in the S configuration



(c) selectively deprotecting the amino group on the  $\delta$  carbon under conditions sufficient to cyclize said ketone to form a cyclic imine and reducing the resulting imine to form a product of the formula in the (S,S) configuration



wherein

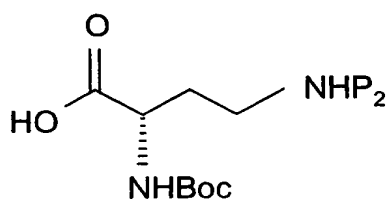
$\text{P}_2$  is an amino protecting group other than Boc,

X is halide.

18. The process according to Claim 17 wherein the amino group on the  $\delta$  carbon is protected by a group that can be removed by hydrogenolysis.

19. The process according to Claim 17 wherein the protecting group on the  $\delta$  amino group on the  $\delta$  carbon is benzyloxycarbonyl.

20. The process of Claim 17 wherein the L-ornithine compound or salt thereof of the formula



is prepared by

- 5 (a) reacting the L-ornithine with a copper salt to form a copper complex with the amino group on the  $\alpha$ -carbon,
- (b) adding a protecting group to the amino group on the  $\delta$  carbon,
- (c) de-complexing the copper, and
- (d) reacting the product of (c) with Boc anhydride in the presence of an inorganic
- 10 base.

21. The process of Claim 20 wherein the copper salt is copper sulfate pentahydrate.

22. The process of Claim 20 wherein the amino group on the  $\delta$  carbon is protected by

15 CBZ.

23. The process according to Claim 1 wherein in step (a) base is additionally present.

24. The process according to Claim 23 wherein the base is triethylamine, diisopropyl ethylamine, 2,6-lutidine, N, N,N', N'-tetramethylethylenediamine, potassium carbonate, lithium carbonate, sodium hydroxide, potassium hydroxide or N-methylmorpholine.

5 25. The process according to Claim 17 wherein the Grignard reagent is phenyl magnesium bromide, phenyl magnesium chloride or phenyl magnesium iodine.

26. The process according to Claim 17 wherein from 3-6 equivalents of Grignard reagent is used per amide.

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27. The process according to Claim 26 wherein about 4.0 to about 4.5 equivalents of Grignard reagent is used relative to the amide.

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28. The process of Claim 17 wherein the reduction of the cyclic imine is effected by catalytic hydrogenation.

29. The process of Claim 28 wherein the catalyst is palladium on carbon.

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30. The process of Claim 28 wherein the reduction of cyclic imine is conducted in a solvent and the solvent is methanol.

31. The process of Claim 17 wherein the deprotection of the amino group on the  $\delta$  carbon is performed at the same time as imine formation and reduction.

32. The process according to Claim 20 wherein the inorganic base is sodium carbonate, sodium bicarbonate, potassium carbonate, potassium hydroxide, sodium hydroxide, potassium fluoride or barium hydroxide.

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